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found in original claims 30-35, in the Specification at page 7, lines 4-17, page 10, lines 15-21, and page 39, lines 5-16. Claims 40 - 48 have been added. Support for the addition of Claims 40 - 48 may be found in the Specification at page 7, lines 4-7, 18-30, page 11, lines 9-16 at page 18, and lines 11-19 and page 38, lines 13-15. An Appendix of Pending Claims is attached for the Examiner's convenience.

### **Claim Objections**

Claims 4-22 have been objected to because they recited the limitation "claim 1." Claims 4-22 have been canceled. Applicants respectfully request the withdrawal of the objection.

### **Rejection under 35 U.S.C. § 112, first paragraph**

Claims 19-23 are rejected under 35 U.S.C. § 112, first paragraph. Without admitting the propriety of the rejection and reserving the right to pursue these claims at a later date, Claims 19-23 have been canceled. Applicants respectfully request withdrawal of the rejection.

### **Rejection under 35 U.S.C. § 112, second paragraph**

Claims 2-35 are rejected under 35 U.S.C. § 112, second paragraph. Without admitting the propriety of the rejection and reserving the right to pursue these claims at a later date, Claims 2-29 have been canceled. Claims 30-35 have been amendeed. Applicants respectfully request withdrawal of the rejection.

### **Rejection under 35 U.S.C. § 102(b)**

Claims 23-28 are rejected under 35 U.S.C. 102(b) as being anticipated by Hardman (U.S. Patent No. 4,939,666). Without admitting the propriety of the rejection and reserving the right to pursue these claims at a later date, Claims 23-28 have been cancelled. Applicants respectfully request the rejection under 35 U.S.C. § 102(b) be withdrawn.

### **Rejection under 35 U.S.C. § 103 (a)**

Claims 24-29 are rejected under 35 U.S.C. § 103(a) over Hardman in view of Lee (U.S. Patent No. 5,241,470). Without admitting the propriety of the rejection and reserving

the right to pursue these claims at a later date, Claims 24-29 have been cancelled. Applicants respectfully request the rejection under 35 U.S.C. § 103(a) be withdrawn.

**DOUBLE PATENTING**

**35 U.S.C. §101**

Claims 2-17 and 19-29 are provisionally rejected under 35 U.S.C. § 101 as claiming the same invention as that of claims 2-27 and 38 of co-pending application 09/837,886.

Without admitting the propriety of the rejection and reserving the right to pursue these claims at a later date, Claims 2-17 and 20-29 have been cancelled. Applicants respectfully request withdrawal of the rejection.

Claims 24-29 are provisionally rejected under 35 U.S.C. § 101 as claiming the same invention as that of claims 22-27 of co-pending Application 09/714,357. Without admitting the propriety of the rejection and reserving the right to pursue these claims at a later date, Claims 24-29 have been cancelled. Applicants respectfully request withdrawal of the rejection.

Claims 2-29 are provisionally rejected under 35 U.S.C. § 101 as claiming the same invention as that of claims 2-29 and 31 of co-pending Application 09/714,357. Without admitting the propriety of the rejection and reserving the right to pursue these claims at a later date, Claims 2-29 have been cancelled. Applicants respectfully request the withdrawal of the rejection.

Claims 6-10 and 21-17 are rejected under 35 under 35 U.S.C. § 101 as claiming the same invention as that of claims 2-15 of prior U.S. Patent No. 6,188,965. Without admitting the propriety of the rejection and reserving the right to pursue these claims at a later date, Claims 2-20 have been cancelled. Applicants respectfully request withdrawal of the rejection.

**Non-statutory Double Patenting Rejection**

Claim 2, 6, 11, and 19-22 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 2, 6, 11 and 19-22 of U.S. Patent No. 6,269,312. Without admitting the propriety of the rejection and reserving the right to pursue these claims at a later date, Claims 2, 6, 11, and 19-22 have been cancelled. Applicant's respectfully request withdrawal of the non-statutory obvious-type double patenting rejection.

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The Applicants submit that in light of the above-amendment and argument, the claims are now in condition for allowance and an early notification of such is respectfully solicited.

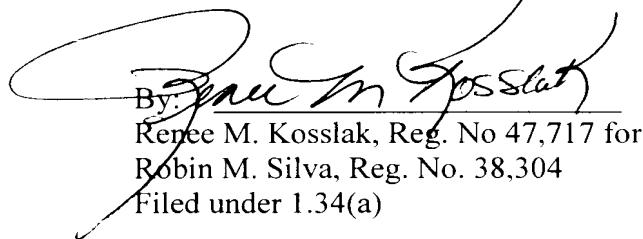
Attached hereto is a marked-up version of the changes made to the claims by the "Amendment". The attached page is captioned "**Version with markings to show changes made.**"

Please direct any calls in connection with this application to the undersigned at (415) 781-1989.

Dated: 11/25/02

Respectfully submitted,

GORSEY & WHITNEY, LLP

  
By: Renee M. Kosslek  
Renee M. Kosslek, Reg. No 47,717 for  
Robin M. Silva, Reg. No. 38,304  
Filed under 1.34(a)

Four Embarcadero Center  
Suite 3400  
San Francisco, California 94111-4187  
Telephone: (415) 781-1989  
Fax No. (415) 398-3249



VERSION WITH MARKINGS TO SHOW CHANGES MADE

Claims 2-29 have been canceled.

Claim 30 has been amended as shown below:

30. (Once Amended) A computer readable memory that upon execution by a computer processor carries out the following functions:

- a) alters at least one supersecondary structure parameter value of a protein backbone structure;
- b) correlates a group of potential rotamers for residue positions of said protein backbone structure; and
- c) analyzes the interaction of each of said rotamers with all or part of the remainder of said protein backbone structure to generate a set of optimized protein sequences.

Claim 31 has been amended as shown below:

31. (Once Amended) A computer readable memory according to claim [30] 39 wherein said ranking module includes a van der Waals scoring function component.

Claim 32 has been amended as shown below:

32. (Once Amended) A computer readable memory according to claim [30] 39 wherein said ranking module includes an atomic solvation scoring function component.

Claim 33 has been amended as shown below:

33. (Once Amended) A computer readable memory according to claim [30] 39 wherein said ranking module includes a hydrogen bond scoring function component.

Claim 34 has been amended as shown below:

34. (Once Amended) A computer readable memory according to claim [30] 39 wherein said ranking module includes a secondary structure scoring function component.

Claim 35 has been amended as shown below:

35. (Once Amended) A computer readable memory according to claim [30] 39 that further assess the correspondence between potential energy test results and theoretical potential energy data.

## Appendix of Pending Claims

30. (Once Amended) A computer readable memory that upon execution by a computer processor carries out the following functions:

- a) alters at least one supersecondary structure parameter value of a protein backbone structure;
- b) correlates a group of potential rotamers for residue positions of said protein backbone structure; and
- c) analyzes the interaction of each of said rotamers with all or part of the remainder of said protein backbone structure to generate a set of optimized protein sequences.

31. (Once Amended) A computer readable memory according to claim 39 wherein said ranking module includes a van der Waals scoring function component.

32. (Once Amended) A computer readable memory according to claim 39 wherein said ranking module includes an atomic solvation scoring function component.

33. (Once Amended) A computer readable memory according to claim 39 wherein said ranking module includes a hydrogen bond scoring function component.

34. (Once Amended) A computer readable memory according to claim 39 wherein said ranking module includes a secondary structure scoring function component.

35. (Once Amended) A computer readable memory according to claim 39 that further assess the correspondence between potential energy test results and theoretical potential energy data.

36. (New) A computer readable memory that upon execution by a computer processor carries out the following functions:

- a) alters at least one supersecondary structure parameter value of a protein backbone structure;
- b) correlates a group of potential amino acids for residue positions of said protein backbone structure; and

c) analyzes the interaction of each of said amino acids with all or part of the remainder of said protein backbone structure to generate a set of optimized protein sequences.

37. (New) A computer readable memory that upon execution by a computer processor carries out the following functions:

- a) alters at least one structure parameter value of a protein backbone structure;
- b) correlates a group of potential rotamers for residue positions of said protein backbone structure; and
- c) analyzes the interaction of each of said rotamers with all or part of the remainder of said protein backbone structure to generate a set of optimized protein sequences.

38. (New) A computer readable memory that upon execution by a computer processor carries out the following functions:

- a) alters at least one structure parameter value of a protein backbone structure;
- b) correlates a group of potential amino acids for residue positions of said protein backbone structure; and
- c) analyzes the interaction of each of said amino acids with all or part of the remainder of said protein backbone structure to generate a set of optimized protein sequences.

39. (New) A computer readable memory according to claims 30, 36, 37, or 38 wherein said analyzing step comprises a ranking module.

40. (New) A computer readable memory that upon execution by a computer processor carries out the following functions:

- (A) receiving a protein backbone structure with variable residue positions;
- (B) altering at least one supersecondary structure parameter value of said protein backbone structure prior to establishing a group of potential amino acids;
- (C) establishing a group of potential amino acids for each of said variable residue positions, wherein a first group for a first variable position has a first set of at least two amino acid side chains, and wherein a second group for a second variable position has a second set of at least two different amino acid side chains; and

(D) analyzing the interaction of all or part of each of said amino acids with all or part of the remainder of said protein backbone structure to generate a set of optimized protein sequences.

41. (New) A computer readable memory according to claim 40 wherein said first and second sets of amino acids are different.

42. (New) A computer readable memory according to claim 40 wherein said first and second sets of amino acids are the same.

43. (New) A computer readable memory that upon execution by a computer processor carries out the following functions:

- a) receiving a protein backbone structure with variable residue positions;
- b) altering at least one supersecondary structure parameter value of said protein backbone structure prior to establishing a group of potential \*residue positions;
- c) establishing a group of potential rotamers for each of said variable residue positions, wherein the group for at least one variable residue position has rotamers of at least two different amino acid side chains, and wherein at least one of said amino acid side chains is from a hydrophilic amino acid; and,
- d) analyzing the interaction of each of said rotamers with all or part of the remainder of said protein to generate a set of optimized protein sequences, wherein said analyzing step includes the use of at least one scoring function.

44. (New) A computer readable memory according to claim 43 wherein said first and second sets of rotamers are different.

45. (New) A computer readable memory according to claim 43 wherein said first and second sets of rotamers are the same.

46. (New) A computer readable memory according to claim 43 wherein said hydrophilic amino acid is selected from the group consisting of serine, threonine, aspartic acid, asparagine, glutamine, glutamic acid, arginine, lysine, and histidine.

\*47. (New) A computer readable memory according to claims 40 or 43 wherein said

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analyzing step comprises a ranking module.

48. (New) A computer readable memory according to claims 30-47 further comprising physically generating at least one member of said set of optimized protein sequences and experimentally testing said sequence for a desired function.